Subretinal Human Retinal Progenitor Cells (hRPC) in Retinitis Pigmentosa (RP)

A Phase I/IIa update

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Relevant disclosure

- Consultant to ReNeuron PLC

Full disclosures available in conference program

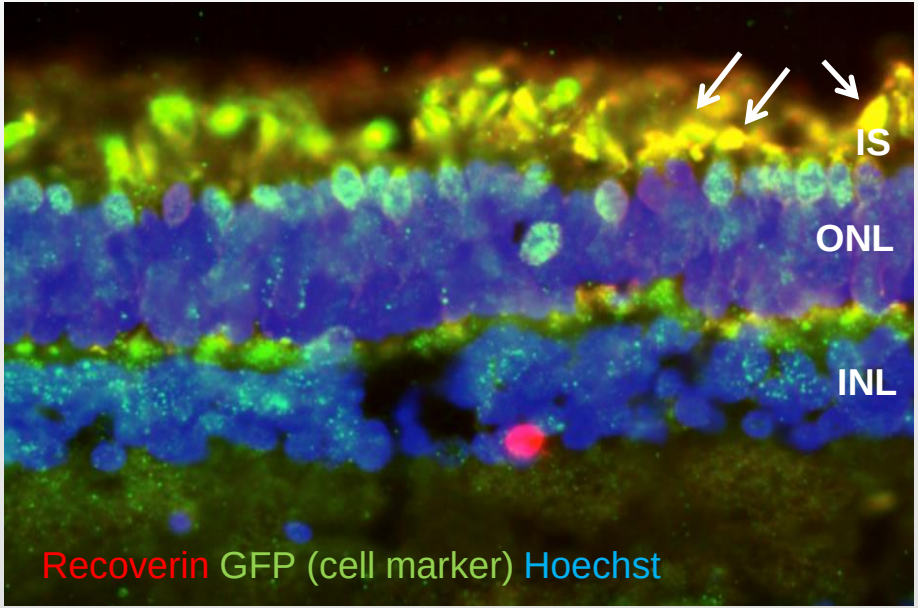
ReNeuron’s retinal progenitor cell (hRPC) therapy

- Cells isolated from fetal retina
- Can differentiate into retinal cells
- Cryopreserved with 9 month shelf life
- No immunosuppression required

Baranov et al (2014)

Mechanism of Action

Allogeneic transplantation in pigs @ 4 wks post-injection



Abud et al (2015)

Both integration and paracrine effects may contribute to efficacy

Subretinal hRPC

Potential benefits

1 *Direct delivery into subretinal space*

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2 *On demand shipment to site of care*

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1 *Direct delivery into subretinal space*

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2 *On demand shipment to site of care*

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3 *Treatment agnostic to genetic subtype of disease*

RP Phase I/IIa clinical trial (NCT02464436)

Open-label, single, unilateral, subretinal injection of hRPC (worse eye)

Phase I study design

Subjects (N=12)

Baseline:
ETDRS letters: 0-1***
VA: LP - 20/800

****only 1 patient read 1 letter*

Dose

250K*, 500K*, 1M** cells

**fresh; **cryopreserved*

Safety Endpoint

Good safety profile allowed progression into Phase IIa#

US Clinical Site:
Massachusetts Eye & Ear, Boston, Jason Comander, MD, PhD

 # Data presented by Dr. Comander in April 2019, at Retinal Cell and Gene Therapy Innovation Summit (Vancouver, BC).

RP Phase I/IIa clinical trial (NCT02464436)

Open-label, single, unilateral, subretinal injection of hRPC (worse eye)

Study ongoing

Phase IIa study design

Subjects (N=10)

Baseline:
ETDRS letters: 9-56
VA: 20/640-20/80

Dose

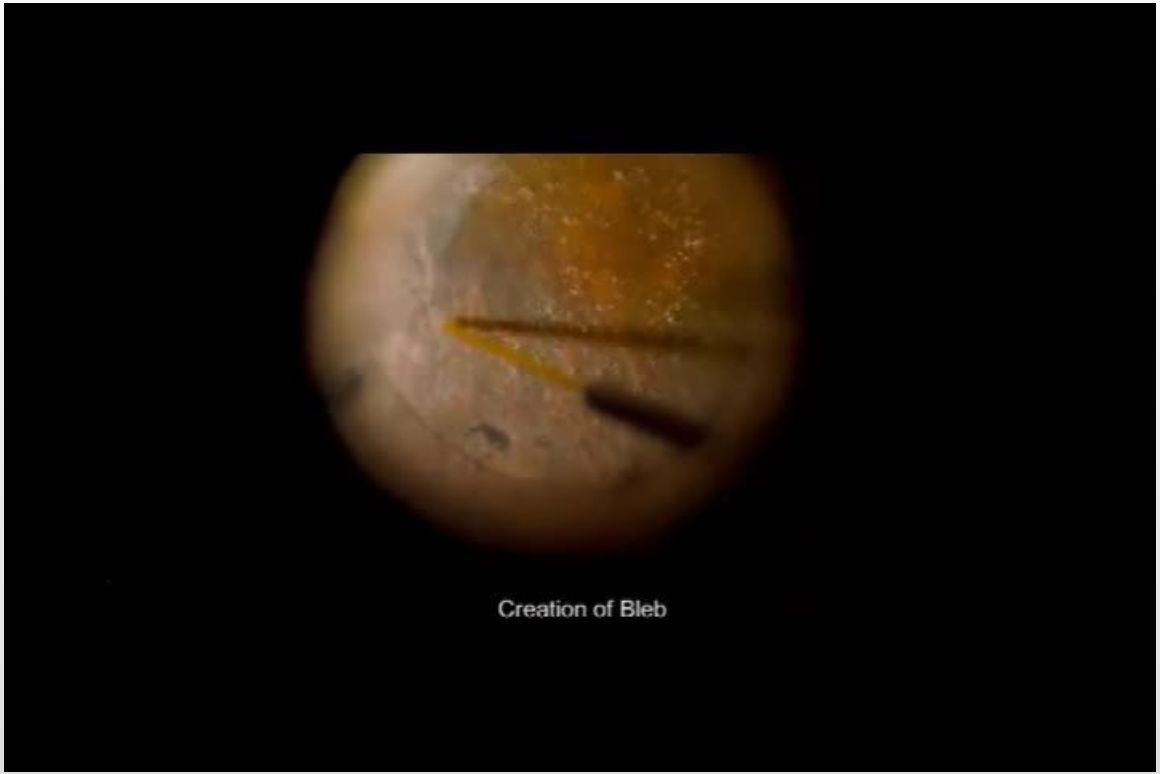
1M cells in cryopreserved formulation

Primary Endpoint

Change in ETDRS letters read from baseline to 24 months post-treatment
(Interim visits: 1, 2, 3, 6, 9, 12, 18 months)

US Clinical Sites:
Massachusetts Eye & Ear, Boston, Jason Comander, MD, PhD
Retinal Research Institute, Phoenix, Pravin Dugel, MD

Surgical Procedure



Phase I/IIa safety

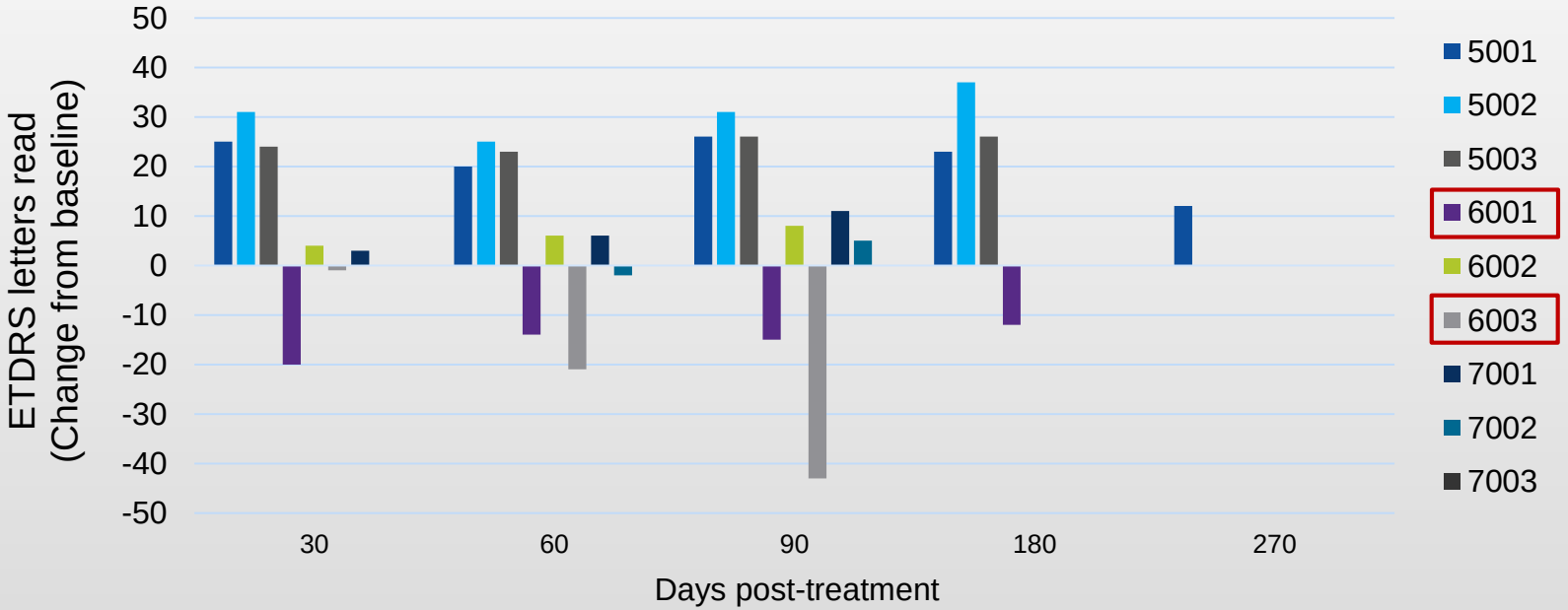
- N=22 subjects
- Dose escalation generally well-tolerated
- No evidence of inflammation or proliferative vitreoretinopathy
- 2 ocular SAEs reported – not related to drug product
  - Subject 4001 - progression of pre-existing epiretinal membrane requiring additional surgery
  - Subject 6003 - persistent subretinal fluid/patent retinotomy

Phase I/IIa safety

- 2 events leading to vision loss (one AE, one SAE) related to surgical procedure/patient selection
  - Subject 6001 – RPE tear
  - Subject 6003 – persistent subretinal fluid/patent retinotomy

ETDRS letters read: Phase IIa portion

Change from baseline in treated eye

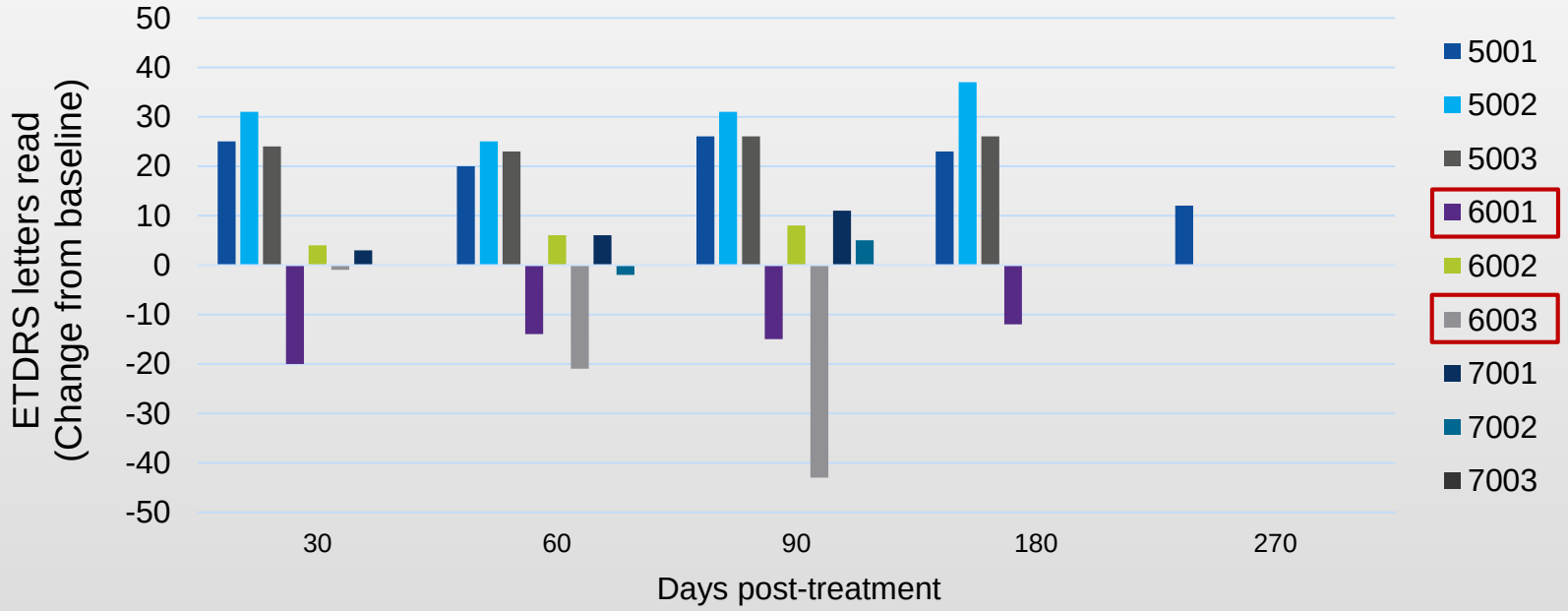


ETDRS letters read: Phase IIa portion

Change from baseline in treated eye

Mean change:
(per timepoint)

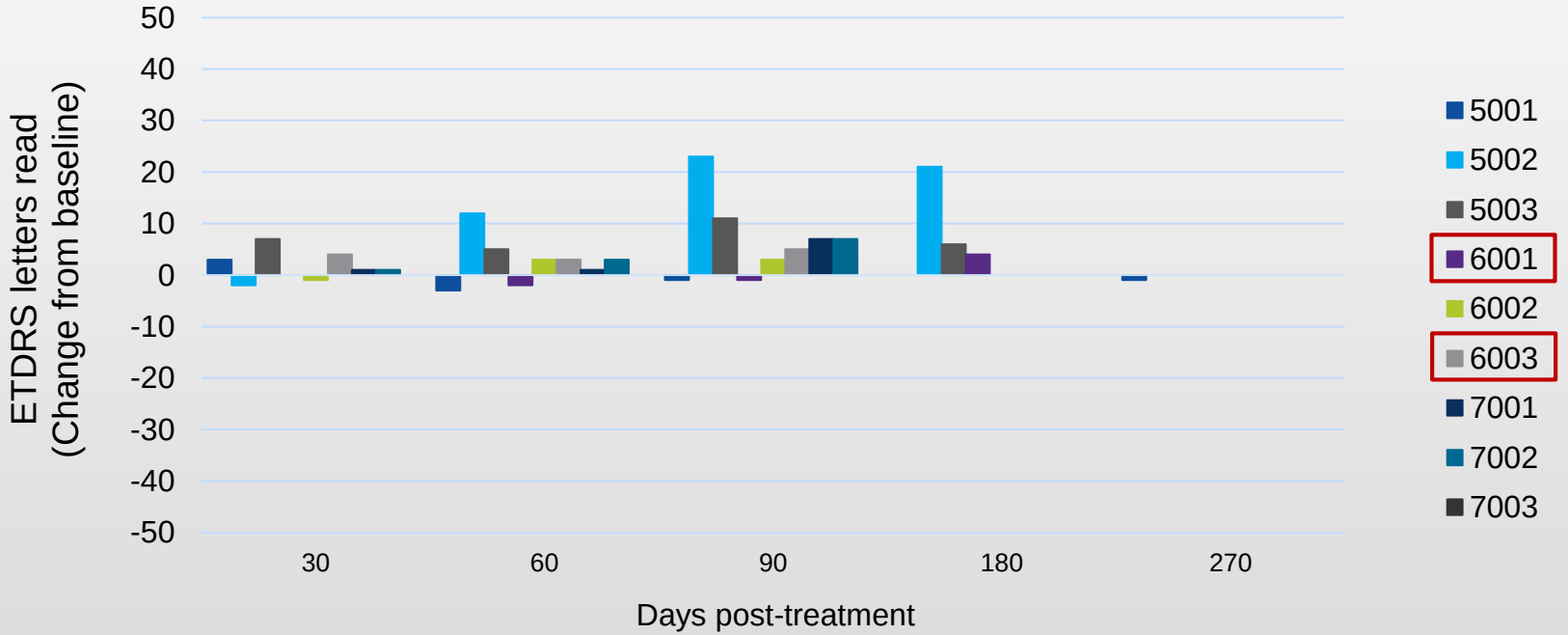
+8.3 (n=8) *+5.4 (n=8)* *+6.1 (n=8)* *+18.5 (n=4)* *+12 (n=1)*



ETDRS letters read: Phase IIa portion

Change from baseline in untreated eye

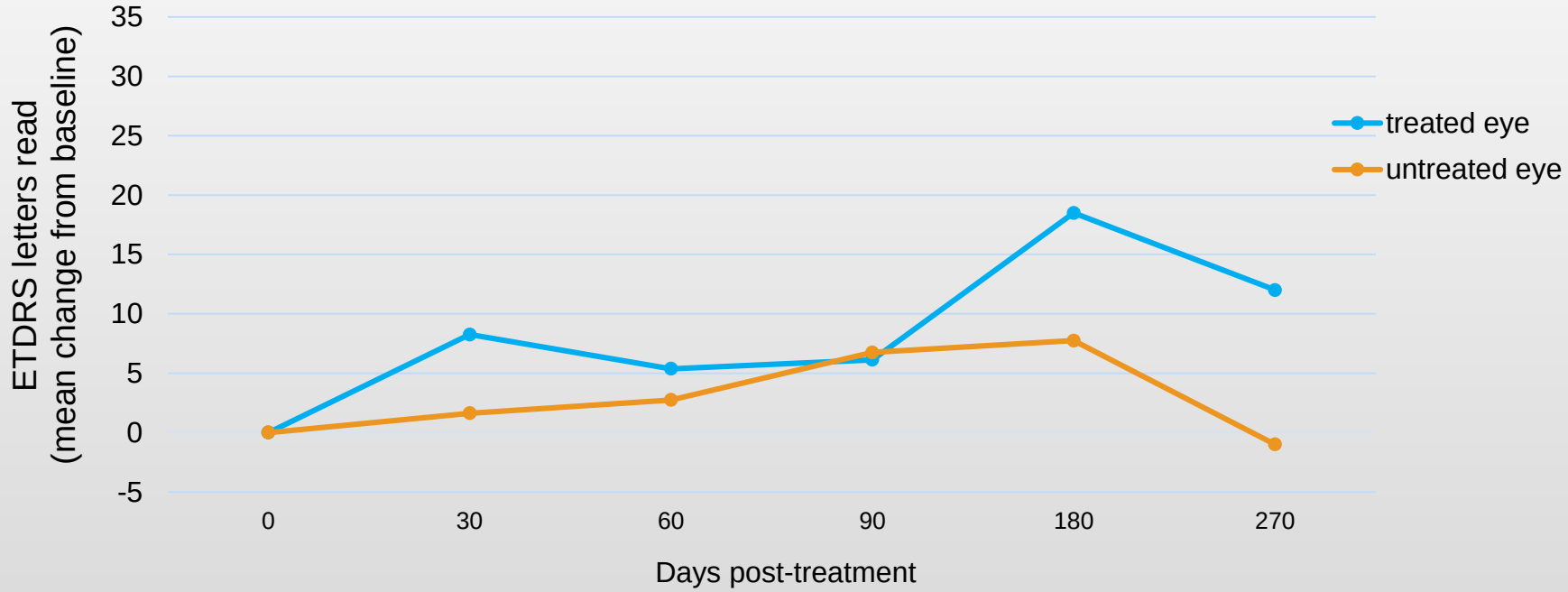
Mean change: *(per timepoint)* *+1.6 (n=8)* *+2.8 (n=8)* *+6.8 (n=8)* *+7.8 (n=4)* *-1 (n=1)*



ETDRS letters read: Phase IIa portion

Mean changes in treated eye vs untreated eye

Mean change: *(per timepoint)*	*+8.3 (n=8)*	*+5.4 (n=8)*	*+6.1 (n=8)*	*+18.5 (n=4)*	*+12 (n=1)*	*treated eye*
	+1.6 (n=8)	*+2.8 (n=8)*	*+6.8 (n=8)*	*+7.8 (n=4)*	*-1 (n=1)*	*untreated eye*

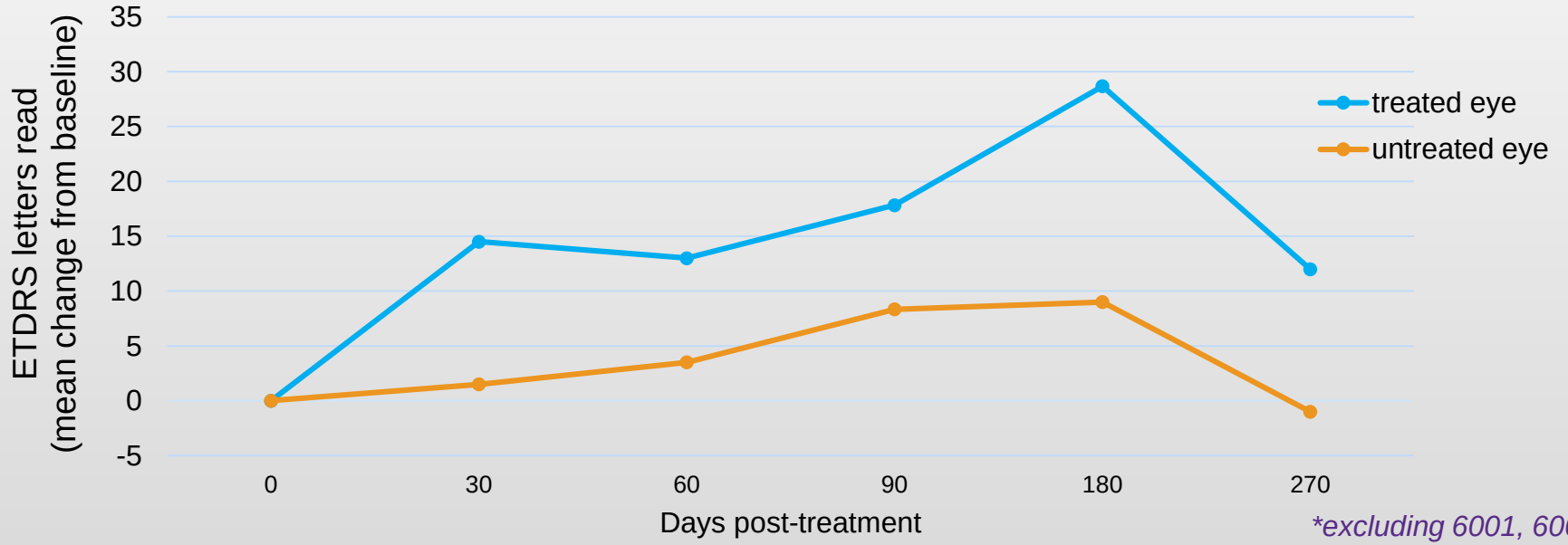


ETDRS letters read: Phase IIa portion

Mean changes in treated eye vs untreated eye

Subjects with vision loss excluded

Mean change:* *(per timepoint)*	*+14.5 (n=6)*	*+13 (n=6)*	*+17.8 (n=6)*	*+28.7 (n=3)*	*+12 (n=1)*	*treated eye*
	+1.5 (n=6)	*+3.5 (n=6)*	*+8.3 (n=6)*	*+9.0 (n=3)*	*-1 (n=1)*	*untreated eye*



**excluding 6001, 6003*

Summary

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  - Very rapid and profound in some patients
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Summary

- Acceptable safety profile
- Biological efficacy signals
  - Very rapid and profound in some patients
  - Slower in other patients
- These study results will provide a better understanding of optimal patient selection and surgical procedure standardization for future study design
- Potentially a promising new therapy for patients with RP